Graduate Schools
Infection Immunity and Cancer, UniGe & UniL: CUS
Biology & Medicine, CMU

Seminar in Microbiology

Monday, December 18th, 2017

Salle de séminaire, E07.3347.a, CMU

11:30 – 12:30

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Phage therapy for *Staphylococcus aureus*: who, how, when… and when not.

Selected publications:

http://www.virologyhighlights.com/whats-in-a-russian-phage-cocktail/

Sarker SA, Sultana S, Reuteler G, Moine D, Descombes P, Charton F, Bourdin G, **McCallin S**, Ngom-Bru C, Neville T, Akter M, Huq S, Qadri F, Talukdar K, Kassam M, Delley M, Loiseau C, Deng Y, El Aidy S, Berger B, Brüssow H. 2016. Oral Phage Therapy of Acute Bacterial Diarrhea With Two Coliphage Preparations: A Randomized Trial in Children From Bangladesh. EBioMedicine. 4:124-37

McCallin S, Alam Sarker S, Barretto C, Sultana S, Berger B, Huq S, Krause L, Bibiloni R, Schmitt B, Reuteler G, Brüssow H. 2013 Safety analysis of a Russian phage cocktail: from metagenomic analysis to oral application in healthy human subjects. Virology 443:187-96

Sarker SA, **McCallin S**, Barretto C, Berger B, Pittet AC, Sultana S, Krause L, Huq S, Bibiloni R, Bruttin A, Reuteler G, Brüssow H. 2012. Oral T4-like phage cocktail application to healthy adult volunteers from Bangladesh. Virology 434:222-32.

Contact: P.VIOLLIER & P. LINDER

The need for alternative treatments to combat antibiotic resistance is increasing and, with it, phage therapy is gradually (re)gaining attention as such a potential strategy. Bacteriophages have been used clinically for nearly a century in countries of the former USSR, and a recent case-series in the US successfully treated diabetic toe ulcers infected with *Staphylococcus aureus* with a commercial product from Georgia. It is therefore important to understand how Eastern commercial products are designed to target *S. aureus*, and to what extent phages have activity against the diverse antibiotic-resistance spectrum of clinical isolates. Metagenomics was used to identify and compare Staphylococcal phages in nine phage products from Russia and Georgia, as well as screen for genetic safety risks. A single phage component specific for *S. aureus* was detected across all products and manufacturing sights, apart from one product that contained an additional secondary phage. *In vitro* assays indicated a high level of activity of phages against Methicillin Susceptible *S. aureus* (MSSA) and Methicillin Resistant *S. aureus* (MRSA), but underlined an important caveat: an intermediate resistance to vancomycin was significantly associated with reduced phage susceptibility. Infection with a Vancomycin Intermediate *S. aureus* (VISA) isolate is associated with clinical failure, and such antibiotic resistance is conversely the therapeutic indication for which phage therapy is heralded. Further investigations using adsorption assays, qPCR, electron microscopy, and comparative genomics have helped to localize and characterize how phage infection is impeded in VISA isolates, but the answer is not a clear as one might suspect. Exposure to vancomycin caused a decrease in sensitivity to phage, but was maintained long after antibiotic pressure was removed. Mutations in several two-component regulatory systems, as well as in bacterial translation machinery, were associated with phage resistance, although no single mutation alone was sufficient. A larger panel of 25 clinical VISA isolates was analyzed to estimate to what extent phage sensitivity is observed in a hospital setting. Fully understanding vancomycin-induced phage insensitivity will help to define the future therapeutic indications of phage therapy for *S. aureus*.